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EVIC-TOX

DOCUMENT DE
TRAVAIL

4.1

DT.TA.08.Lim.Rat.10/00(1)

Etude : Th 472
Produit : 01-2649

Observation clinique individuelle (OCI)

Date des contrôles - Commentaires

J1 (Juste après le traitement) 17/10/01 8h40 ExN Paraphe : M	J1-T 30 min 9h10 ExN Paraphe : M	J1-T 1h 9h40 OCI Paraphe : M	J1-T 2h 10h40 ExN Paraphe : M
J1-T 3h 11h40 Redistribution nourriture ExN Paraphe : M	J1-T 4h 12h40 ExN Paraphe : M	J1-T 5h 13h40 ExN Paraphe : M	J1-T 6h 14h40 ExN Paraphe : M
J2 18/10/01 ExN Paraphe : M	J3 19/10/01 ExN Paraphe : M	J4 20/10/01 Pesée ExN Paraphe : M	J5 21/10/01 ExN Paraphe : M
J6 22/10/01 ExN Paraphe : M	J7 23/10/01 ExN Paraphe : M	J8 24/10/01 Pesée ExN Paraphe : M	J9 25/10/01 ExN Paraphe : M
J10 26/10/01 ExN Paraphe : M	J11 27/10/01 ExN Paraphe : M	J12 28/10/01 ExN Paraphe : M	J13 29/10/01 ExN Paraphe : M
J14 30/10/01 ExN Paraphe : M	J15 31/10/01 Pesée - Autopsie ExN Paraphe : M		

Après chaque contrôle, parapher dans la case correspondante.

Si examen normal = ExN sinon OCI = observation clinique individuelle (cf fiche d'OCI)

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Etude : Th 472
Produit : 01-2649

Observations cliniques en cage (OC)

DT-TA-OR/Lm-Rat.10/00(1)

Date des contrôles - Commentaires

J1 (juste après le traitement) 17/10/01	J1-T 30 min	J1-T 1h	J1-T 2h
Ex N	Ex N	OCI	Ex N
Paraphe : M	Paraphe : M	Paraphe : M	Paraphe : M
J1-T 3h Redistribution nourriture	J1-T 4h	J1-T 5h	J1-T 6h
Ex N	Ex N	Ex N	Ex N
Paraphe : M	Paraphe : M	Paraphe : M	Paraphe : M
J2 18/10/01	J3 19/10/01	J4 20/10/01	J5 21/10/01
Ex N	Ex N	Pesée Ex N	Ex N
Paraphe : M	Paraphe : M	Paraphe : M	Paraphe : SR
J6 22/10/01	J7 23/10/01	J8 24/10/01	J9 25/10/01
Ex N	Ex N	Pesée Ex N	Ex N
Paraphe : M	Paraphe : M	Paraphe : M	Paraphe : M
J10 26/10/01	J11 27/10/01	J12 28/10/01	J13 29/10/01
Ex N	Ex N	Ex N	Ex N
Paraphe : M	Paraphe : M	Paraphe : SR	Paraphe : M
J14 30/10/01	J15 31/10/01 Pesée - Autopsie		
Ex N	Ex N		
Paraphe : M	Paraphe : M		

Après chaque contrôle, parapher dans la case correspondante.

Si examen normal = Ex N sinon OCI = observation clinique individuelle (cf fiche d'OCI)

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DT.TA. OR.Lim.Rat.10/00(1)

Etude : Th 472
Produit: 01-2649

Observations cliniques individuelles
OC

Rats mâles

N° des animaux	Symptomatologie codifiée*	
	J1-T	Al
7166	E	N
7167	E	N
7168	E	N
7169	E	N
7170	E	N
Date	17/10/01	
Paraphe	M	

Rats femelles

N° des animaux	Symptomatologie codifiée*	
	J1-T	Al
7171	E	N
7172	E	N
7173	E	N
7174	E	N
7175	E	N
Date	17/10/01	
Paraphe	M	

*: codification : cf page 6

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Etude : Th 472
Produit : 01-2649

Observations cliniques
paramètres et codification

DT.TA.OR.Lim.Rat.10/00(1)

Paramètres observés	Symptomatologie	Codification
Examen clinique	Aucune anomalie constatée	Ex N
Activité spontanée (activité motrice)	Toilettage, jeux, alimentation, déplacement augmentés ou diminués	ACTI + ACTI -
Réflexe de Preyer	Absence de réponse à la perception d'un bruit inhabituel (mouvement des pavillons auriculaires et/ou sursauts)	PREY O
Effet respiratoire	Accélération du rythme respiratoire	RESP +
	Diminution du rythme respiratoire	RESP -
	Irrégularité du rythme respiratoire (Apnée)	RESP O
Convulsions	Contractions violentes des muscles - Toniques = continues amenant à une rigidité du corps avec les membres en hyper-extension et décubitus latéral ou dorsal de l'animal. - Cloniques = saccadées interrompues se traduisant par un "pédalage"	TONI + CLON +
Tremblements	Petites oscillations rythmiques involontaires du corps	TREM +
Température	Sensation de chaud ou de froid ressentie par l'expérimentateur au contact de l'animal	TEMP + TEMP -
Tonus musculaire	Etat de tension physiologique des muscles : - hypotonie = diminution du tonus musculaire; l'animal est "mou" - hypertonie = augmentation du tonus se traduisant par une réponse musculaire exagérée au toucher	MUSC - MUSC +
Force de préhension	Aptitude à serrer un objet avec les pattes avant augmentée ou diminuée	FPRE + FPRE -
Ptose palpébrale	Relâchement des paupières se traduisant par une fermeture totale ou une fermeture partielle des paupières	PTOS + PTOS +/-
Mydriase	Dilatation totale de la pupille ou dilatation partielle de la pupille	MYDR + MYDR +/-
Salivation	Sécrétion augmentée de la salive après traitement	SALI +
Larmoiement	Augmentation des larmes après traitement	LARM +
Réflexe de retournement	Perte d'équilibre et de coordination motrice en réponse à une position anormale (animal maintenu sur le dos)	RETO -
Piloérection	Aspect hérissé des poils	PILO +
Diarrhée	Selles liquides	DIAR +
Léthargie	Etat de somnolence prolongée	LETH +
Coma	Perte de conscience, de sensibilité et de mobilité avec conservation relative des fonctions végétatives	COMA +
Modification de la peau	Anomalie constatée au niveau de l'état cutané	PEAU +
Modification du pelage	Anomalie constatée au niveau du pelage	PELA +
Modification des yeux	Anomalie constatée au niveau des yeux	YEUX +
Modification des muqueuses	Anomalie constatée au niveau des muqueuses	MUQU +
Mortalité	Mort naturelle Mort accidentelle Mort par sacrifice	N A S

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Etude : Th 472

Produit : 01-2649

Autopie

N° des animaux	7166	7167	7168	7169	7170
Date de la mort	←	31	10	01	→
Cause de la mort *	MS	MS	MS	MS	MS
Organes observés					
Trachée	O	O	O	O	O
Poumons	O	O	O	O	O
Cœur	O	O	O	O	O
Foie	O	O	O	O	O
Thymus	O	O	O	O	O
Pancréas	O	O	O	O	O
Ganglions lymphatiques	O	O	O	O	O
Rate	O	O	O	O	O
Œsophage	O	O	O	O	O
Estomac	O	O	O	O	O
Duodénum	O	O	O	O	O
Jéjunum	O	O	O	O	O
Ileum	O	O	O	O	O
Cæcum	O	O	O	O	O
Côlon	O	O	O	O	O
Rein gauche	O	O	O	O	O
Rein droit	O	O	O	O	O
Vessie	O	O	O	O	O
Testicule gauche	O	O	O	O	O
Testicule droit	O	O	O	O	O
Paraphe	m	m	m	m	m

Si l'examen est normal mettre O dans la case correspondante

Si l'organe n'est pas observé : mettre / dans la case correspondante

Si l'organe est prélevé : mettre la lettre P dans la case correspondante

* : MS : Animal sacrifié

MN : mort naturelle

MA : mort accidentelle

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PAR LE SERVICE ASSURANCE QUALITÉ
EVIC - FRANCE

Etude : Th 472
Produit : 01-2649

N° des animaux	7171	7172	7173	7174	7175
Date de la mort	←	31	10	01	→
Cause de la mort *	NS	NS	NS	NS	NS
Organes observés					
Trachée	O	O	O	O	O
Poumons	O	O	O	O	O
Cœur	O	O	O	O	O
Foie	O	O	O	O	O
Thymus	O	O	O	O	O
Pancréas	O	O	O	O	O
Ganglions lymphatiques	O	O	O	O	O
Rate	O	O	O	O	O
Œsophage	O	O	O	O	O
Estomac	O	O	O	O	O
Duodénum	O	O	O	O	O
Jéjunum	O	O	O	O	O
Iléon	O	O	O	O	O
Caecum	O	O	O	O	O
Colon	O	O	O	O	O
Rein gauche	O	O	O	O	O
Rein droit	O	O	O	O	O
Vessie	O	O	O	O	O
Paraphe	M	M	M	M	M

Si l'examen est normal mettre O dans la case correspondante
 Si l'organe n'est pas observé : mettre / dans la case correspondante
 Si l'organe est prélevé : mettre la lettre P dans la case correspondante
 * : MS : Animal sacrifié
 MN : mort naturelle
 MA : mort accidentelle

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Etude : Th 472

Produit : 01-2649

Anomalies macroscopiques

Congestion: hyperhémie, excès de sang dans les vaisseaux d'un organe (ou partie d'organe) due à une irritation ou une infection locale (ou artefact de saignée) :

thymus, poumons, intestin grêle / gros intestin, foie, pancréas, rate, ganglions lymphatiques, reins, vessie (muqueuse), ovaires, utérus, vagin.

Hémorragie: effusion de sang hors des vaisseaux en quantité plus ou moins importante (attention à l'artefact d'autopsie).

Sous forme de pétéchies (petits points d'1 mm au maximum de diamètre) ; suffusion = tache hémorragique sur une partie de l'organe.

Anomalies de coloration :

- décoloré, jaune : foie et rein
- blanc / plaques grisâtres : poumons
- léopard : foie

Anomalies de forme :

- dilaté/distendu : estomac, intestin, utérus, rein (bassinets), cœur, vessie
- déformé : bosselé (rein) ; granuleux (rate)
aspect fibreux : traînées blanches et rétractées (rein, foie, rate)
- hypertrophie : augmentation de la taille (et du poids) de l'organe
- atrophie : diminution de la taille (et du poids) de l'organe

Anomalies macroscopiques diverses :

- ulcère/ulcération : estomac, duodénum, œsophage, vagin, vessie (perte de substance plus ou moins profonde de la muqueuse avec sang rouge ou noir) sous forme de points ou traînées.
- formations kystiques : vésicules avec liquide ou substance molle (rein, foie, ovaire).
- abcès : amas de pus dans les tissus (poumons, foie, ganglions ; ou suite à une erreur de voie).
- tissus ou liquides purulents : qui contiennent du pus (poumons ; liquide pleural, péritoine, ascite abdominale).
- tissus d'aspect nécrotique : présentant un aspect de nécrose = mort du tissu.
- points blanc sous-capsulaires : divers points plus ou moins blancs en surface de l'organe, foie ou rein essentiellement (généralement liés à une parasitose).
- adhérences : union de différents organes par des formations fibreuses.
- œdème : infiltration séreuse des muqueuses, des poumons et du tissu cutané,
- mucosités : amas de substances épaisses et filantes en surface des muqueuses.

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Monsieur Benoît LEMAIRE
Botanical extracts dpt
Business Manager
BERKEM
Le Marais Ouest BP 4
24680 GARDONNE

N/Réf. : PG/MCC - N° 02/2353
Subject : Interpretation of
Acute toxicity test

Blanquefort, le 18 octobre 2002

Test reference : Th 452 / 01-2649
Test substance : **CHRYSANTHELLUM** batch 2890
Number of animals : 10 rats (5 males and 5 females)
Administration route : oral route
Dose level : **5000 mg/kg**
Observation period : 14 days after administration
Mortality : 0 %
Symptomatology : none
Necropsy findings : nothing to report

Under the experimental conditions adopted, the substance **CHRYSANTHELLUM** orally administered to 10 rats at the **5000 mg/kg** dose level did not present any acute toxicity signs.



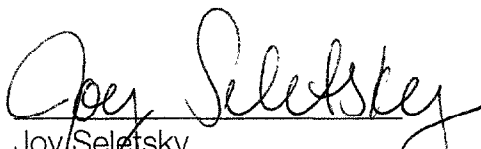
Patrick GOMOND
Directeur d'Etudes

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AFFIDAVIT OF ACCURACY

I, Joy Seletsky, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the following document, "Evaluation of the Acute Toxicity After Oral Administration to the Rat – Limited Testing," from French into English.


Joy Seletsky
TransPerfect Translations, Inc.

1101 Pennsylvania Ave., NW
Washington, DC 20004

Sworn to before me this
16th day of January, 2002


Signature, Notary Public

Lisa Sherfinski
Notary Public, District of Columbia
My Commission Expires 01-01-2008

Stamp, Notary Public

District of Columbia

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EVALUATION OF THE ACUTE TOXICITY AFTER ORAL
ADMINISTRATION TO THE RAT

WORK DOCUMENT 1

– LIMITED TESTING –

DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472

Preparation of the substance

Date: 10/16/01

to be tested (preliminary test)

Initials: [initials]

Product: 01-2649

- Identification of the substance, storage conditions, appearance and organic depressant characteristics

in conformity with the worksheet*

yes X

no ____

* If no, indicate the modifications directly on the worksheet

- Indications provided on the substance:

Solubility:

pH:

Density:

- Substance used as provided by the Sponsor:

yes ____

no X

* If no, complete the table below

Test Results [*Essais réalisés*] [see source for original table]

Vehicle	Quantity of substance weighed (g)	Quantity of vehicle added (g/ml)	Homogenizing (mortar, UltraTurrax, etc.)	Magnetic agitation (yes/no)	Water bath (°C)	Appearance of the final preparation
Water PPI	2g	5ml	No	Yes	No	Thick black liquid
CMC 0.5%						
Corn oil						
Other:						

- Volume selected: 10 ml/kg

Dose selected:

5000 mg/kg

- Substance usage conditions in the study:

Vehicle: EPP[illegible] Cooper

lot 0003

Homogenizing:

- Mortar/rammer

yes no

- UltraTurrax

yes no

- Magnetic agitation

yes X no

Water bath:

yes no X

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If yes, - temperature: _____°C

- Solution preparation method: [handwritten] For 4 kg Animals:
[illegible] Room of [illegible] 20p of product QS 40 ml EPP[illegible]
use [illegible] graduated tube up to 50ml, QS done directly in the tube, manual
agitation using a stainless steel spatula then transfer product to a beaker for the
treatment, apply magnetic agitation for the duration of the treatment [bottom of page
cut off] thick black liquid [illegible] 10-17-01
[illegible]

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EVALUATION OF THE ACUTE WORK DOCUMENT 2
TOXICITY AFTER ORAL
ADMINISTRATION TO THE RAT
- LIMITED TESTING -

Study: Th 472 **Schedule** DT.TA.OR.Lim.Rat.10/00(1)
Product: 01-2649 Date: 10/16/01
Initials: [initials]

Supplier: IFFA-CREDO
Description: SPRAGUE-DAWLEY (EOPS)

[see source for original table]

Month OCTOBER 2001
Day of Month
Day of Test (J) J= Day
Operation

Récp: Receipt of animals (cf Study [illegible] 458) P: Weight of animals D: Hydric diet
Acc: Acclimation OCC: Clinical Observations
T: Treatment OCI: Individual Clinical
Prép: Preparation of the substance Aut: Autopsy
in Cage
Observations

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Study: Th 472

DT.TA.OR.Lim.Rat.10/00(1)

Product: 01-2649

**Body Weight
Treatment**

Time fast started on Day 1 [J-1]: 2:30pm

Time administered on Day 1: 8:30am

Syringe: 2.5 ml

Needle: 15X3'

Male Rats / *Rats mâles*

[see source for original table / numbers]

Number of animals	Marking 1 green ring	Weight at Day 1 (before starting fast) (g)	Weight conforms (yes/no)	Weight at Day 1 /T0 (g)	Final product volume adm./rat (ml)	Weight at Day 4 (g)	Weight at Day 8 (g)	Weight at Day 15 (g)
	Head		Yes					
	Back		Yes					
	Tail		Yes					
	Abdomen		Yes					
	White		Yes					
Total no. of animals								
Average								
Standard deviation								
Total								
Minimal weight								
Maximal weight								
Initials								
Date								

Average weight of male rats: $x = [\text{illegible}]$ gAcceptable limits: $[x-20\%; x+20\%]$

Authorized weight interval: [169.58 at 255.58] g

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Female Rats / *Rats femelles*

[see source for original table / numbers]

Number of animals	Marking 1 green ring	Weight at Day 1 (before starting fast) (g)	Weight in conformity (yes/no)	Weight at Day 1 /T0 (g)	Final product volume adm./rat (ml)	Weight at Day 4 (g)	Weight at Day 8 (g)	Weight at Day 15 (g)
	Head		Yes					
	Back		Yes					
	Tail		Yes					
	Abdomen		Yes					
	White		Yes					
Total no. of animals								
Average								
Standard deviation								
Total								
Minimal weight								
Maximal weight								
Initials								
Date								

Average weight of female rats: $x = [\text{illegible}]$ g Acceptable limits: $[x-20\%; x+20\%]$

Authorized weight interval: [153.52 at 231.52] g

Weight in conformity if falls between the authorized interval (if not, inform the DE, who will decide whether to keep the animal in the test).

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DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472
Product: 01-2649

Clinical Observations in Cage (OCC)

Male Rats

Date of examinations – Comments [*Date des contrôles – Commentaires*]

Day 1 (just after the treatment) 8:40am 10/17/01 Ex N <i>Initials: [initials]</i>	Day 1-T 30 min 9:10am Ex N <i>Initials: [initials]</i>	Day 1-T 1 hour 9:40am OCI Ex N <i>Initials: [initials]</i>	Day 1-T 2 hr 10:40am Ex N <i>Initials: [initials]</i>
Day 1-T 3 hr 11:40am Redistribution of food Ex N <i>Initials: [initials]</i>	Day 1-T 4 hr 12:40pm Ex N <i>Initials: [initials]</i>	Day 1-T 5 hr 1:40pm Ex N <i>Initials: [initials]</i>	Day 1-T 6 hr 2:40pm Ex N <i>Initials: [initials]</i>
Day 2 10/18/01 Ex N <i>Initials: [initials]</i>	Day 3 10/19/01 Ex N <i>Initials: [initials]</i>	Day 4 10/20/01 Weighing Ex N <i>Initials: [initials]</i>	Day 5 10/21/01 Ex N <i>Initials: [initials]</i>
Day 6 10/22/01 Ex N <i>Initials: [initials]</i>	Day 7 10/23/01 Ex N <i>Initials: [initials]</i>	Day 8 10/24/01 Weighing Ex N <i>Initials: [initials]</i>	Day 9 10/25/01 Ex N <i>Initials: [initials]</i>
Day 10 10/26/01 Ex N <i>Initials: [initials]</i>	Day 11 10/27/01 Ex N <i>Initials: [initials]</i>	Day 12 10/28/01 Ex N <i>Initials: [initials]</i>	Day 13 10/29/01 Ex N <i>Initials: [initials]</i>
Day 14 10/30/01 Ex N <i>Initials: [initials]</i>	Day 15 10/31/01 Weighing – Autopsy Ex N <i>Initials: [initials]</i>		

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After each examination, initial the corresponding box.

If the examination is normal = Ex N If not OCI = Individual Clinical Observation (cf OCI form)

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DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472
Product: 01-2649

**Clinical Observations in Cage (OCC)
Female Rats**

Date of examinations – Comments [*Date des contrôles – Commentaires*]

Day 1 (just after the treatment) 10/17/01 Ex N <i>Initials: [initials]</i>	Day 1-T 30 min Ex N <i>Initials: [initials]</i>	Day 1-T 1 hour OCI Ex N <i>Initials: [initials]</i>	Day 1-T 2 hr Ex N <i>Initials: [initials]</i>
Day 1-T 3 hr Redistribution of food Ex N <i>Initials: [initials]</i>	Day 1-T 4 hr Ex N <i>Initials: [initials]</i>	Day 1-T 5 hr Ex N <i>Initials: [initials]</i>	Day 1-T 6 hr Ex N <i>Initials: [initials]</i>
Day 2 10/18/01 Ex N <i>Initials: [initials]</i>	Day 3 10/19/01 Ex N <i>Initials: [initials]</i>	Day 4 10/20/01 Weighing Ex N <i>Initials: [initials]</i>	Day 5 10/21/01 Ex N <i>Initials: [initials]</i>
Day 6 10/22/01 Ex N <i>Initials: [initials]</i>	Day 7 10/23/01 Ex N <i>Initials: [initials]</i>	Day 8 10/24/01 Weighing Ex N <i>Initials: [initials]</i>	Day 9 10/25/01 Ex N <i>Initials: [initials]</i>
Day 10 10/26/01 Ex N <i>Initials: [initials]</i>	Day 11 10/27/01 Ex N <i>Initials: [initials]</i>	Day 12 10/28/01 Ex N <i>Initials: [initials]</i>	Day 13 10/29/01 Ex N <i>Initials: [initials]</i>
Day 14 10/30/01 Ex N <i>Initials: [initials]</i>	Day 15 10/31/01 Weighing – Autopsy Ex N <i>Initials: [initials]</i>		

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After each examination, initial the corresponding box.

If the examination is normal = Ex N If not OCI = Individual Clinical Observation (cf OCI form)

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EVALUATION OF THE ACUTE WORK DOCUMENT 5
TOXICITY AFTER ORAL
ADMINISTRATION TO THE RAT
- LIMITED TESTING -

DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472

Product: 01-2649

Individual Clinical Observations

OCI

Male Rats / *Rat mâles*

No. of animals Codified symptomatology*
Day 1-T 1 hr

[see source for original numbers and entries]

Date 10/17/01

Initials M

Female Rats / *Rats femelles*

No. of animals Codified symptomatology*
Day 1-T 1 hr

[see source for numbers and entries]

Date 10/17/01

Initials M

*: codification: cf page 6

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DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472
Product: 01-2649

Clinical Observations:
Parameters and Codification

Observed Parameters	Symptomatology	Codification
Clinical Examination	No anomalies noted	Ex N
Spontaneous Activity (Motor activity)	Grooming, playing, eating, movement increased	ACTI +
	or decreased	ACTI -
Preyer's Reflex	Absence of response to perception of an unusual noise (movement of auricles and/or jumping)	PREY 0
Respiratory effect	Acceleration of respiratory rhythm	RESP +
	Diminution of respiratory rhythm	RESP -
	Irregularity of respiratory rhythm	RESP 0
	(Apnea)	
Convulsions	Violent muscle contractions -Tonic: continuous, leading to body rigidity with members hyper-extended and animal lying on its side or back	TONI +
	- Clonic: spasmodic, interrupted, indicated by "pedaling"	CLON +
Trembling	Small involuntary rhythmic oscillations of the body	TREM +
Temperature	Sensation of heat	TEMP +
	or of cold, felt by the experimenter in contact with the animal	TEMP -
Muscle tone	Physiological state of muscle tension: - hypotonia = diminution of muscle tone; the animal is "soft"	MUSC -
	- hypertonia = increase in tone, indicated by an exaggerated muscular response to touching	MUSC +
Prehensile strength	Aptitude at gripping an object with the front paws – increased	FPRE +
	or decreased	FPRE -
Palpebral ptosis	Relaxation of the eyelids indicated by	PTOS +

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	complete closure	
	or partial closure of the eyelids	PTOS +/-
Mydriasis	Total dilation of the pupil	MYDR +
	or partial dilation of the pupil	MYDR +/-
Salivation	Increased secretion of saliva after treatment	SALI +
Lacrimation	Increase in secretion of tears after treatment	LARM +
Turnover [reversal] reflex	Loss of equilibrium and motor coordination in response to an abnormal position (animal stays on its back)	RETO -
Pilo-erection	Fur standing on end	PILO +
Diarrhea	Liquid stools	DIAR +
Lethargy	State of prolonged somnolence	LETH +
Coma	Loss of consciousness, sensitivity and mobility with relative conservation of vegetative functions	COMA +
Modification of skin	Anomaly noted on condition of skin	PEAU +
Modification of fur	Anomaly noted on condition of fur	PELA +
Modification of eyes	Anomaly noted on condition of eyes	YEUX +
Modification of mucus linings	Anomaly noted on condition of mucus linings	MUQU +
Mortality	Natural death	N
	Accidental death	A
	Sacrificial death	S

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EVALUATION OF THE ACUTE WORK DOCUMENT 7.1
TOXICITY AFTER ORAL
ADMINISTRATION TO THE RAT
– LIMITED TESTING –

DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472
Product: 01-2649 Autopsy
Male Rats

[see source for numbers and entries]

No. of animals

Date of death

Cause of death*

Organs observed

Trachea
Lungs
Heart
Liver
Thymus
Pancreas
Lymph nodes
Spleen
Esophagus
Stomach
Duodenum
Jejunum
Ileum
Caecum
Colon
Left kidney
Right kidney
Bladder
Left testicle
Right testicle
Initials

If the examination is normal, put O in the corresponding box

If the organ is not observed: put / in the corresponding box

If the organ has been removed, put the letter P in the corresponding box

**MS: animal sacrificed*

MN: natural death

MA: accidental death

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EVALUATION OF THE ACUTE WORK DOCUMENT 7.2
TOXICITY AFTER ORAL
ADMINISTRATION TO THE RAT
– LIMITED TESTING –

DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472

Product: 01-2649

Autopsy
Female Rats

[see source for numbers and entries]

No. of animals

Date of death

Cause of death*

Organs observed

Trachea

Lungs

Heart

Liver

Thymus

Pancreas

Lymph nodes

Spleen

Esophagus

Stomach

Duodenum

Jejunum

Ileum

Caecum

Colon

Left kidney

Right kidney

Bladder

Initials

If the examination is normal, put O in the corresponding box

If the organ is not observed: put / in the corresponding box

If the organ has been removed, put the letter P in the corresponding box

**MS: animal sacrificed*

MN: natural death

MA: accidental death

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DT.TA.OR.Lim.Rat.10/00(1)

Study: Th 472

Product: 01-2649

**Autopsy – Glossary of
Macroscopic Signs**

Congestion: hyperthermia, excess of blood in the vessels of an organ (or part of an organ) due to an irritation or a local infection (or evidence of bleeding):

Thymus, lungs, small intestine / large intestine, liver, pancreas, spleen, lymph nodes, kidneys, bladder (mucus lining), ovaries, uterus, vagina.

Hemorrhage: pooling of blood outside the vessels in more or less significant quantities (attention to evidence of autopsy).

In the form of petechial hemorrhages (small spots of 1 mm maximum diameter); suffusion = hemorrhaging area on one part of the organ.

Anomalies of coloration:

- Discolored, yellow: liver and kidney
- White / gray areas: lungs
- Leopard spots: liver

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Anomalies of shape:

- Dilated / distended: stomach, intestine, uterus, kidney (renal), heart, bladder
- Deformed: dented (kidney); granular (spleen)
Fibrous appearance: white and elevated streaks (kidney, liver, spleen)
- Hypertrophy: increase in size (and in weight) of the organ
- Atrophy: diminution in size (and in weight) of the organ

Miscellaneous macroscopic anomalies:

- Ulcer / ulceration: stomach, duodenum, esophagus, vagina, bladder (more or less significant loss of substance of mucus lining with black or red blood) in the form of spots or streaks.
- Cystic formations: vesicles with liquid or soft substance (kidney, liver, ovary).
- Abscess: accumulation of pus in the tissues (lungs, liver, ganglions; or following a misdirection).
- Purulent tissues or liquids: which contain pus (lungs: pleural liquid, peritoneum, abdominal ascites).
- Tissues with a necrotic appearance: showing a necrotic aspect = dead tissues.

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- White sub-capsular spots: various more or less white spots on the surface of the organ, mainly the liver or kidney (generally associated with a parasitosis).
- Adherences: joining of different organs by fibrous formations.
- Edema: serous infiltration of the mucus linings, lungs and skin tissue.
- Mucus: accumulation of thick and stringy substances on the surface of the mucus linings.

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